“Adventures with computer simulations of biomolecules in cellular environments”

Abstract: A primary role of computer simulations in biology is to complement high-resolution structural data from experiments with a dynamic perspective and ultimately connect to and explain biological function. Continuing challenges are how to reach biologically relevant time scales but also how to embrace the full biological complexity of cellular environments. Recent studies that highlight how both challenges can be addressed in modern simulations are presented. In the first example, the fundamental process of transcription in RNA polymerase II is analyzed via a combination of molecular dynamics simulations and kinetic network modeling to span a wide range of time scales. The results provide new insights into the mechanism by which RNA polymerase can achieve high RNA elongation rates while keeping errors due to nucleotide misincorporation to a minimum. The second example involves models at different levels of complexity of crowded cellular environments up to a comprehensive model of a bacterial cytoplasm and recently generated high-resolution models of genomic bacterial DNA. These systems were studied via molecular dynamics simulations to examine how such environments may affect the stability and dynamics of biological macromolecules. The simulations are discussed in the context of experimental measurements and how to bridge between the molecular-level views to system-wide quantitative studies.